

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

APPLICANT(S):      Kaufman et al.

SERIAL NO.:          Continuation of      ART UNIT:          Not yet assigned  
                         U.S.S.N. 09/738,614

FILING DATE:        Herewith              EXAMINER:          Not yet assigned

TITLE:                METHODS FOR PROCESSING SEQUENTIAL IMAGES OF A  
                         SAMPLE

**PRELIMINARY AMENDMENT**

Box Patent Application  
Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to calculation of the filing fee for the above-identified continuation application, Applicants respectfully request entry of this Amendment.

In the Specification:

Please delete the section under the heading "Cross Reference to Related Applications" and replace with the replacement section as set forth in the attached marked up version of the amended Cross Reference to Related Applications section to read as set forth in the replacement Cross Reference to Related Applications section in clean form.

In the Claims

Please add new claims 33-60 and cancel without prejudice claims 1-32 prior to calculating the filing fee.

Please add new claims 33-60 as follows:

33. (NEW) A method of correlating sequential images obtained from a sample, said method comprising the steps of,
- locally applying a chemical agent to a sample,
  - obtaining a plurality of sequential images of said sample, and
  - processing at least two of said sequential images to correlate said at least two sequential images.
34. (NEW) The method of claim 33, wherein said locally applying step comprises topically applying said chemical agent to said sample.
35. (NEW) The method of claim 33, wherein said locally applying step comprises locally injecting of said chemical agent into said sample.
36. (NEW) The method of claim 33, wherein said processing step comprises compensating for misalignment between said at least two sequential images.
37. (NEW) The method of claim 33, wherein said processing step comprises compensating for image deformations between said at least two sequential images.
38. (NEW) The method of claim 33, wherein said processing step comprises compensating for a relative motion between said sample and a detection device.
39. (NEW) The method of claim 33, wherein said processing step comprises aligning said at least two sequential images using a feature present in each of said at least two sequential images.
40. (NEW) The method of claim 33, wherein the processing step comprises,
- constructing a compensation map based at least in part on a change in position of a feature present in each of said at least two sequential images, and
  - aligning said feature present in each of said at least two sequential images using said compensation map.

41. (NEW) The method of claim 33, wherein one or more of said plurality of sequential images comprise measurements of an optical signal produced by said sample.
42. (NEW) The method of claim 41 wherein, said optical signal comprises a light spectrum.
43. (NEW) The method of claim 42, wherein said light spectrum comprises a fluorescence spectrum.
44. (NEW) The method of claim 41, wherein said optical signal is produced by an endogenous chromophore.
45. (NEW) The method of claim 44, wherein said endogenous chromophore comprises a molecule selected from a group consisting of NADH, collagen, elastins, flavins, hemoglobins, and porphyrins.
46. (NEW) The method of claim 33, wherein said sample comprises human cervical tissue.
47. (NEW) The method of claim 33, wherein said sample is selected from a group consisting of colorectal tissue and gastric tissue.
48. (NEW) The method of claim 33, wherein said chemical agent interacts with said sample to alter an optical signal produced by said sample.
49. (NEW) The method of claim 33, wherein said chemical agent is selected from a group consisting of acetic acid, formic acid, propionic acid, and butyric acid.
50. (NEW) The method of claim 33, wherein said chemical agent is selected from a group consisting of Lugol's iodine, Shiller's iodine, methylene blue, toluidine blue, and indigo carmine.
51. (NEW) The method of claim 33, wherein said processing step comprises,

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processing at least two of said sequential images to produce image compensation information, and

correlating said at least two sequential images using said image compensation information.

52. (NEW) The method of claim 51 further comprising, using said image compensation information to process one or more optical signals from said sample.
53. (NEW) The method of claim 52, wherein said optical signal comprises a fluorescence spectrum.
54. (NEW) The method of claim 33 further comprising, determining a characteristic of an area of said sample based at least in part on one or more of said at least two sequential images subsequent to correlation.
55. (NEW) The method of claim 54, wherein said determining step comprises evaluation of at least one morphological feature of said area.
56. (NEW) The method of claim 55, wherein said at least one morphological feature is selected from the group consisting of size, shape, and border sharpness.
57. (NEW) The method of claim 54, wherein said determining step comprises using a Reid index.
58. (NEW) The method of claim 54, wherein said determining step is further based on a change in an optical signal from said area of said sample.
59. (NEW) The method of claim 54, wherein said area of said sample comprises human cervical tissue, and said characteristic of said area of human cervical tissue comprises abnormal health.

60. (NEW) An article of manufacture having computer-readable program means with computer-readable instructions embodied thereon for performing the method of claim 33.

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**REMARKS**

Claims 1-32 were originally filed in application serial no. 09/738,614. Applicants add new claims 33-60 and cancel without prejudice claims 1-32. As a result, claims 33-60 will be pending after entry of this Amendment. In accordance with 35 U.S.C. § 1.121, attached is a clean copy of all pending claims.

No new matter is added by claims 33-60. Applicants submit that support for new claims 33-60 is found throughout the specification and at least at page 5, lines 5-13, and pages 46-64.

In addition, Applicants amend the specification under the Cross Reference to Related Applications section to insert the proper claim for priority and serial numbers of referenced patent applications. Applicants submit that no new matter is introduced by these amendments. In accordance with 35 U.S.C. § 1.121, attached is a marked up version of the replacement section and a copy of the replacement section in clean form.

If it is believed that a telephone conversation with Applicants' attorney would be helpful in expediting prosecution of this, the subject application, the Examiner is invited to call the undersigned.

Respectfully submitted,



Michael J. Bastian

Registration No. 47,411

Attorney for Applicants

Tel. (617) 248-7102

Fax (617) 248-7100

Dated: February 5, 2002

TESTA, HURWITZ & THIBEAULT, LLP

High Street Tower

125 High Street

Boston, MA 02110

bastiamj6219/19.2277440-1

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**MARKED UP VERSION OF AMENDED**

**CROSS REFERENCE TO RELATED APPLICATIONS SECTION**

This application claims priority to and the benefit of U.S. patent application Serial No. 09/738,614, filed December 15, 2000, and U.S. patent application Serial No. 09/738,147, filed December 15, 2000, both of which claim priority to and benefit of U.S. provisional patent application Serial No. 60/170,972, filed December 15, 1999, the entire disclosures of which applications are hereby incorporated by reference.

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**REPLACEMENT CROSS REFERENCE**  
**TO RELATED APPLICATIONS SECTION IN CLEAN FORM**

This application claims priority to and the benefit of U.S. patent application Serial No. 09/738,614, filed December 15, 2000, and U.S. patent application Serial No. 09/738,147, filed December 15, 2000, both of which claim priority to and benefit of U.S. provisional patent application Serial No. 60/170,972, filed December 15, 1999, the entire disclosures of which applications are hereby incorporated by reference.

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**CLEAN COPY OF ALL PENDING CLAIMS**

33. A method of correlating sequential images obtained from a sample, said method comprising the steps of,
- locally applying a chemical agent to a sample,
- obtaining a plurality of sequential images of said sample, and
- processing at least two of said sequential images to correlate said at least two sequential images.
34. The method of claim 33, wherein said locally applying step comprises topically applying said chemical agent to said sample.
35. The method of claim 33, wherein said locally applying step comprises locally injecting of said chemical agent into said sample.
36. The method of claim 33, wherein said processing step comprises compensating for misalignment between said at least two sequential images.
37. The method of claim 33, wherein said processing step comprises compensating for image deformations between said at least two sequential images.
38. The method of claim 33, wherein said processing step comprises compensating for a relative motion between said sample and a detection device.
39. The method of claim 33, wherein said processing step comprises aligning said at least two sequential images using a feature present in each of said at least two sequential images.
40. The method of claim 33, wherein the processing step comprises,
- constructing a compensation map based at least in part on a change in position of a feature present in each of said at least two sequential images, and
- aligning said feature present in each of said at least two sequential images using said compensation map.

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43. The method of claim 42, wherein said light spectrum comprises a fluorescence spectrum.
44. The method of claim 41, wherein said optical signal is produced by an endogenous chromophore.
45. The method of claim 44, wherein said endogenous chromophore comprises a molecule selected from a group consisting of NADH, collagen, elastins, flavins, hemoglobins, and porphyrins.
46. The method of claim 33, wherein said sample comprises human cervical tissue.
47. The method of claim 33, wherein said sample is selected from a group consisting of colorectal tissue and gastric tissue.
48. The method of claim 33, wherein said chemical agent interacts with said sample to alter an optical signal produced by said sample.
49. The method of claim 33, wherein said chemical agent is selected from a group consisting of acetic acid, formic acid, propionic acid, and butyric acid.
50. The method of claim 33, wherein said chemical agent is selected from a group consisting of Lugol's iodine, Shiller's iodine, methylene blue, toluidine blue, and indigo carmine.
51. The method of claim 33, wherein said processing step comprises,  
processing at least two of said sequential images to produce image compensation information, and

correlating said at least two sequential images using said image compensation information.

52. The method of claim 51 further comprising, using said image compensation information to process one or more optical signals from said sample.
53. The method of claim 52, wherein said optical signal comprises a fluorescence spectrum.
54. The method of claim 33 further comprising, determining a characteristic of an area of said sample based at least in part on one or more of said at least two sequential images subsequent to correlation.
55. The method of claim 54, wherein said determining step comprises evaluation of at least one morphological feature of said area.
56. The method of claim 55, wherein said at least one morphological feature is selected from the group consisting of size, shape, and border sharpness.
57. The method of claim 54, wherein said determining step comprises using a Reid index.
58. The method of claim 54, wherein said determining step is further based on a change in an optical signal from said area of said sample.
59. The method of claim 54, wherein said area of said sample comprises human cervical tissue, and said characteristic of said area of human cervical tissue comprises abnormal health.
60. An article of manufacture having computer-readable program means with computer-readable instructions embodied thereon for performing the method of claim 33.